**In the Specification:**

Please amend the specification as shown:

Please delete paragraph [0034] and replace it with the following paragraph:

Figure 14A-D. Simulation of Reactive Sequencing of [CTGA] GAA ACC AGA AAG TCC [T] **(SEQ ID NO: 1)**, probed with a dNTP cycle. 14A **(SEQ ID NO: 7)**. Sequence readout close to the primer where no extension failure has occurred. 14B **(SEQ ID NO: 7)**. Sequence readout downstream of primer where 60% of the strands have undergone extension failure and are producing out of phase signals and misincorporation has prevented extension on 75% of all strands. 14C **(SEQ ID NO: 7)**. Downstream readout with error signals from trailing strands (dark shading) distinguished from correct readout signals from leading strands (light shading) using knowledge of the downstream sequence of the trailing strands. 14D **(SEQ ID NO: 7)**. Corrected sequence readout following subtraction of error signals from trailing strands. Note the similarity to the data of Fig. 1A.

Please delete paragraph [0035] and replace it with the following paragraph:

Figure 15 **(SEQ ID NO: 8)**. Effect of a leading strand population on extension signals.

Please delete paragraph [0126] and replace it with the following paragraph:

An experiment was performed to demonstrate efficient fluorescent detection **and destruction of** fluorophore using a template sequence. The template, synthesized with a al**kylamino linker at the 5'** terminus,

was:

3'-$H_2N$-$(CH_2)_7$-GAC CAT TAT AGG TCT TGT TAG GGA AAG GAA GA 5' **(SEQ ID NO: 2)**

Please delete paragraph [0127] and replace it with the following paragraph:

The trial sequence to be determined is: G GGA AAG GAA GA **(SEQ ID NO: 3)**.

Please delete paragraph [0128] and replace it with the following paragraph:

A tetramethyrhodamine-labeled primer sequence was synthesized to be co**mplementary to the template as** follows:

5'-[Rhodamine]-$(CH_2)_6$-CTG GTA ATA TCC AGA ACA AT- **3' (SEQ ID NO: 4)**

Please delete paragraph [0161] and replace it with the following paragraph:

Figures 14A and 14B demonstrate how data would appear for a sequence: [CTGA] GAA ACC AGA AAG T CC [T] **(SEQ ID NO: 1)**, probed with a dNTP cycle: CAGT, close to the primer where no extension failure has occurred (Figure 14A) and well downstream (Figure 14B) at a point where 60% of the strands have undergone extension failure and are producing out-of-phase signals, and misincorporation has shut down extension on 75% of all strands. The readouts shown start at the second G in the sequence (beyond the [CTGA] sequence in parentheses) and end at the last C (before the [T] in parentheses). The digital nature of the signal in Figure 14A and also the amplitude scale should be noted. In Figure 14B, the signal for a single base extension has been reduced by 60%, from 1.0 to 0.4 due to the misincorporation and the resulting 75% Signal loss. However, added to the correct extension signals are signals due to the out-of-phase extension of the trailing strands. At first sight, the readout is completely different from the correct readout shown in Figure 14A, due to the superposition of signals produced when the trailing strands encounter the sequence previously traversed by the leading strands. Particularly large errors arise whenever the trailing strand population encounters the AAA repeats. For example, the second T probe yields a signal amplitude corresponding to an AAAAA repeat instead of the correct signal A, the third G probe gives a signal corresponding to CCC

when in fact there is no C at this point in the leading strand sequence, the fourth T probe reads 4 A's when the correct sequence has none (the trailing strands encounter the second AAA repeat). However, because the sequence from the leading strands is known, the false signals arising from the trailing strands can be predicted and subtracted from the total signal to obtain the correct sequence readout. This is shown in Figure 14C, where the signals arising from the trailing strands are coded by different shading from the leading strand signal. Because the signals due to the trailing strands can be predicted, the error signals can be subtracted to obtain the correct digital sequence readout shown in Figure 14D. It should be noted that the data in Figure 14D are now identical to those in Figure 14A, and yield the correct sequence readout for the leading strands, the only difference being that the overall intensity is reduced due to the assumed loss of signal due to Misincorporation and extension failure, the latter populating the trailing strands. In other words, by keeping track of the sequence in a computer the effect is as though one could directly visualize the different contributions as depicted on the plot in Figure 14C. Therefore, it is possible to predict for any probe nucleotide event exactly what the signal from the trailing strand population should be, and subtract this error signal from the measured signal to arrive at a true digital signal representative of the sequence of the leading strand population, which is the desired result.

Please delete paragraph [0165] and replace it with the following paragraph:

Optimization of reagents, enzymes and reaction conditions should allow misincorporation probabilities below 1%, and extension failure probabilities as low as 0.1%. The computer aided monitoring method of the present invention additionally provides a means for healing the trailing strand population by selectively extending this population so that it is again synchronous with the leading strands. For example, given a dNTP probe cycle of GCTA, and a template sequence (beyond the 3' end of the primer) of:

.....GTGCAGATCTG... (SEQ ID NO: 5)

and assuming that when dCTP is in the reaction chamber, the polymerase fails to incorporate a C in some fraction of the primer strands, the following results:

| | |
|---|---|
| Template | .....GTG CAG ATC TG... (SEQ ID NO: 5) |
| Main strands | .....C |
| Template | .....GTG CAG ATC TG (SEQ ID NO: 5) |
| Failure strands | ..... |

At the end of the first cycle, the main strands have extended by...CA, while the failure strand has not advanced. After one more complete cycle, the main strand extension is....CAC and the failure strand now reads....CA, i.e. now just one base out of phase.

| | |
|---|---|
| Template | .....CTG CAG ATC TG... (SEQ ID NO: 5) |
| Main strands | .....CAC |
| Template | .....CTG CAG ATC TG... (SEQ ID NO: 5) |
| Failure strands | .....CA |

Because the phase lag arises from the repeating interaction of the probe cycle sequence with the template sequence, the unchanged probe cycle can never have the correct sequence to resynchronize the strand. Instead, if the probe cycle is unchanged, and if no further extension failures occur, the phase lag for a given failure strand osicillates perpetually between 1 and 3 bases, counting single base repeats as one base for this purpose. However because the leading strand sequence up to the last extension is always known, one can determine the effect of introducing an extension failure at some upstream position. It should be noted that an extension failure introduced at any arbitrary upstream position, or any base type, always produces the same phase lag because the effect of an extension failure is to cause extension of the affected strand to lag by one complete dNTP cycle. Thus, it is possible to alter the probe cycle sequence, for example to probe with a C, instead of a G, after the last A in the sequence discussed above. The failure strand would advance while the main strands did not and the phase lag would heal. In yet another

**embodiment the dNTP** probe cycle may be reversed whenever the phase lag shrinks to only 1 base. **Whenever the phase** difference declines to a single base, or repeats of a single base, then simply **reversing the probe cycle** sequence always resynchronizes the strands.

Please delete paragraph [0166] and replace it with the following paragraph:

Figure 15 shows how a leading strand population arising from incorrect extension of a fraction of primer strands due to nucleotide impurities can adversely affect the signals from the main population. Using the same template sequence as before: [CTGA] GAA ACC AGA AA GT C C [TC AGT] **(SEQ ID NO: 6)** and the same probe cycle: CAGT, the effect of a leading strand population which is 20% of the main strand population can be simulated and 2 bases ahead of the main strands at the time the main strand sequence begins to be read. The leading strands have already extended by -C TTT. The first C probe extends the main primer strands by one base complementary to the first G in the sequence giving a single base extension signal of 1. The first G extends the leading strands by -GG- complementary to the -CC-repeat, giving a signal of 0.4. Greater ambiguity arises when the leading strands encounter the second AAA-repeat at the second T probe, increasing the main strand signal from the correct value for a single base extension to 1.6. In the absence of further information, this value will be ambiguous or may be interpreted as a 2-base repeat.